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ORIGINAL RESEARCH

Size tuning and oxygen plasma induced pore formation on silica nanoparticles

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Abstract Silica nanoparticles have been prepared from tetraethylorthosilicate dissolved in ethanol followed by base-catalyzed condensation. Earlier works reported that at least four parameters, namely concentration of tetraethylorthosilicate, ethanol, water and ammonia solution are needed to be optimized for the size tuning of silica nanoparticles. In this work size tuning of 5 nm–250 nm has been achieved by varying a single synthesis parameter i.e., the concentration of ammonia solution. Oxygen plasma was found to be successful for generating pores on silica nanoparticles without using any structure directing agents. The properties and morphology of nanoparticles were investigated by transmission electron microscopy, scanning electron microscopy, energy dispersive X- ray spectroscopy and Fourier transformed infrared spectroscopy.

1. Introduction

Silica nanoparticles (SNPs) occupy an outstanding position in scientific field due to their enormous applications in catalysis, electronics and thin film substrates, separation technology, sensor technology, pharmacy and agriculture [1–9]. Many research works have also been carried out on the use of SNPs for targeted drug delivery both in medicine and agriculture [10–16]. In order to put SNPs into application for targeted drug delivery, the minimization of particle size to nanometer range is critical since most of the cellular uptake occurs within the size ranging from 5 nm to 250 nm in both animal and plant cells [11,16,17].

Significant research progress has been made in controlling and modifying the properties of mesoporous silica materials since its discovery [18–21]. Stober et al. reported a pioneer method for the synthesis of spherical and monodisperse SNPs from aqueous alcohol solutions of silicon alkoxides using ammonia as a catalyst

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[22]. Bogush and Zukoski prepared monodispersed silica particles from 40 nm to several micrometers by controlled hydrolysis of tetraethylorthosilicate (TEOS) in ethanol followed by condensation of the dispersed phase material [23]. Other approaches for the preparation of highly monodispersed silica nanospheres involved the use of basic amino acid monomers instead of ammonia [24,25] and elemental silicon instead of other expensive precursors [26]. The influence of synthesis conditions such as solution composition and temperature on the formation of SNPs was systematically investigated. The characteristics of mesoporous silica at different aging-temperature and the behavior of this system on the microencapsulation of a model drug were also investigated [27].

S.K. Park et al. and G. L. Davies et al. reported the optimization of four different experimental parameters, including concentration of silica source and NH_3 solution, type of solvent and reaction temperature for controlling the size and size distribution of SNPs [28,29]. In contrast to these earlier research reports of size tuning, the study on the control of the nanoparticle size for developing SNPs has been carried out in the present investigation, and the experimental results showed that the concentration of NH_3 solution can be the only deciding parameter for developing SNPs with the size ranging from 5 nm to 250 nm, keeping all other synthesis conditions constant.

Porous SNPs could open up wide possibilities in drug delivery system [11,30–32]. Their unique architecture of having parallel pores with two openings allows them to be filled with suitable drugs for controlled release and provide opportunities for designing zero premature release systems, which could be operated under the control of various external physical or chemical stimuli [33–35]. The common methods for developing highly porous SNPs involve the use of suitable surfactants or structure directing agents, such as cetyltrimethyl ammonium bromide (CTAB) followed by their removal by acid wash or calcination [16,36,37]. However there were some reports regarding the toxicity of surfactants such as CTAB to cells while using them as stabilizing agent for the nanomaterial used for cellular delivery [38–40]. If such agents are involved in the synthesis of mesoporous SNPs, failure in their complete removal might produce cell toxicity while using such porous SNPs as drug delivery vectors. Hence it is better if we could create pores on the surface of SNPs without using any surfactant agents. Plasma treatment has reported to be a promising way to remove organic templates and generate mesoporous thin films. Compared to conventional thermal calcination methods, plasma treatment provides a promising low-temperature, low cost and time saving preparation process. Studies regarding the use of argon and oxygen plasma for generating mesopores on silica thin films have been reported [41–44]. On the basis of this, we tried to generate pores on spherical SNPs by plasma method. We had used oxygen plasma as direct etching tool for inducing pores on SNPs without using any structure directing agents, and this method is proved to be very easy and time saving.

The characterization of SNPs was carried out using transmission electron microscopy (TEM), scanning electron microscopy (SEM), energy dispersive spectroscopy (EDS) and Fourier transformed-infrared (FT-IR) spectroscopy.

2. Experimental

For the synthesis of SNPs, we had used TEOS as the silica source, NH_3 solution as the catalyst, Ethanol (EtOH) as the solvent (all from Kanto Chemical Co., Japan) and distilled water. All chemicals were used as received without further purification. SNPs were synthesized following the base catalyzed condition via hydrolysis of TEOS and condensation reaction. TEOS, H_2O and EtOH were taken at a molar ratio of 1:53.6:40.7 respectively and ammonia solution was added at varying concentration. TEOS (5 ml) and EtOH (40 ml) were taken in a conical flask and mixed vigorously using a magnetic stirrer for 10 min at 60 °C. Different concentrations of ammonia solution (6, 8, 12, 16, 20 and 24% v/v) were prepared for each experiment and added dropwise to TEOS-EtOH solution under constant stirring followed by refluxing for 3 h at a constant temperature of 60 °C. White colored silica nanopowder was dried out of the solution with rotary evaporator and stored in air tight glass bottles. The synthesized nanoparticles were subjected to characterization for determination of size, shape and its chemical nature.

TEM image was recorded with JEM-2200-FS Field Emission Microscope at an accelerating voltage of 200 KV and electron diffraction study was conducted to check the nature of the sample. Energy dispersive X-ray spectroscopy (EDS) analysis and EDS mapping were carried out using JED 2300 attached with JEM-2200-FS Field Emission Microscope for chemical characterization of the synthesized nanoparticles. The morphology of the particle was analyzed by SEM using JEOL JSM-7400 F Field Emission Scanning Electron Microscope operated at 5 KV accelerating voltage. The sample on specimen stubs were coated with platinum (approximately 50 nm thickness) using Hitachi E-1030 ion sputter machine before microscopic examination. FTIR spectrum was recorded on a Shimadzu IR Prestige-21 in diffused reflectance, operating at a resolution of 4 cm^{-1}.

The characterized nanoparticles were subjected to plasma treatment to generate pores on their surface by direct etching method using Samco Basic Plasma Kit Model BP 1. Detailed description of this plasma kit was given in a work already published from authors' laboratory [45], i.e. the apparatus consisted of a Pyrex glass bell jar and a pair of parallel disk electrodes (70 mm in diameter). The lower electrode was connected to a heater and the upper one was connected to a RFG-200 radio-frequency generator operated at 13.56 MHz, through an impedance-matching circuit. A thin layer of SNPs (around 100 nm in size) was prepared on a clean glass slide. The glass slide was then carefully placed on the lower electrode. Direct pore formation was initially tried with argon plasma at a flow rate of 5 ml/min at 20 °C without any sample heating. Plasma power and processing time varied from 100–200 W and 30 min to 1 h, respectively. The same treatment was again conducted by heating the samples to 150 °C inside the reactor. The whole experiment was repeated with oxygen plasma instead of argon plasma by maintaining a flow rate of 60 ml/min at 20 °C both without and with sample heating of 150 °C. The chamber pressure was kept at 20 Pa during the whole procedure. The treated samples were then subjected to the characterization using TEM and SEM.

3. Results and discussion

SNPs of size ranging from 5 nm to 250 nm have been successfully synthesized by modifying the Stober process. On keeping all other synthesis conditions and parameters constant (as mentioned earlier in the introduction part), size tuning was

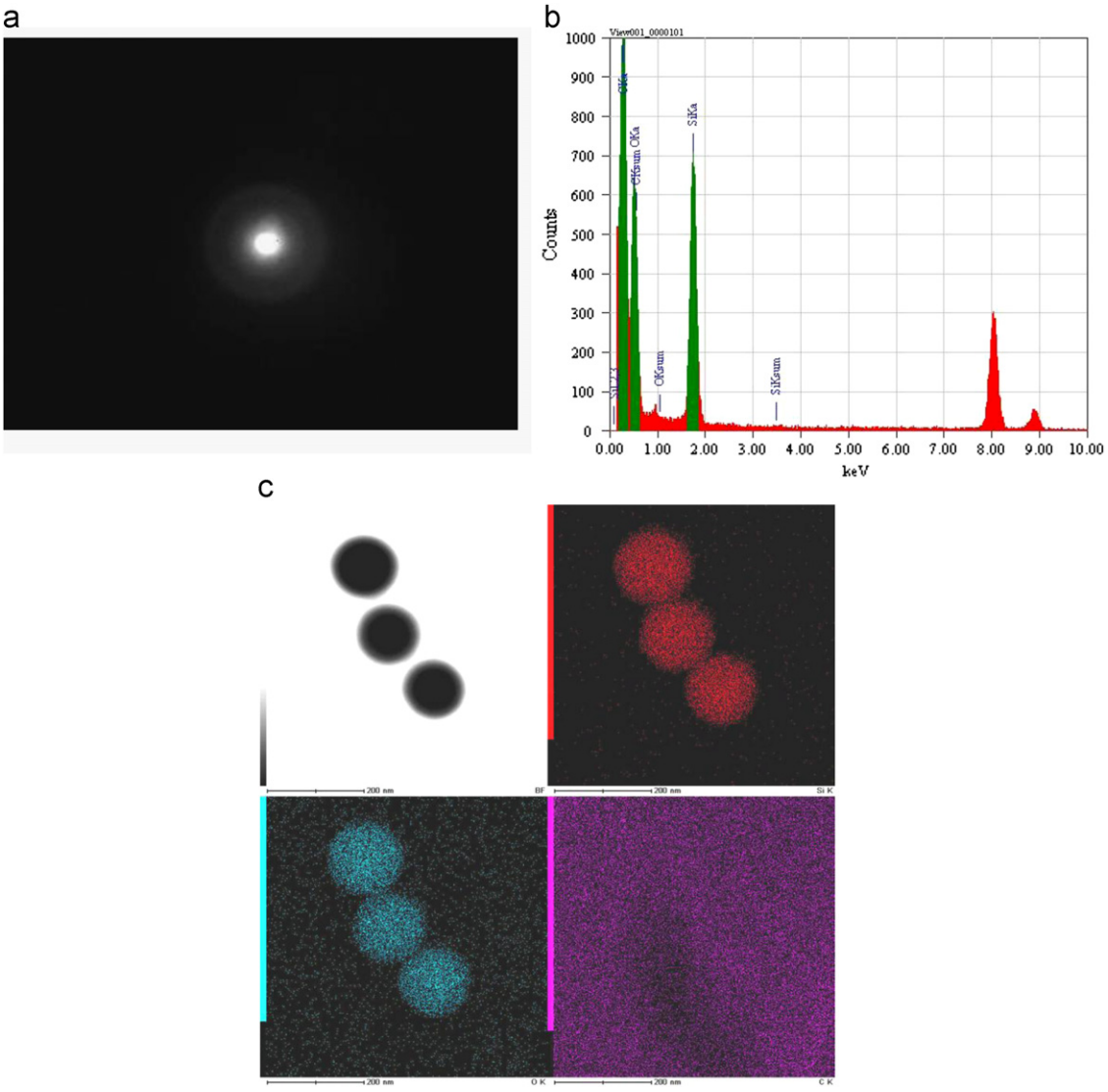

Fig. 1 (a) Diffraction pattern of SNPs. The ring structure confirmed the amorphous nature of the sample. (b) EDS analysis of SNPs. We have obtained only three elements C, O and Si. (c) EDS mapping of SNPs. Red color—Silicon, Blue color—Oxygen and Pink color—Carbon. Carbon comes from the supporting film used for TEM analysis.

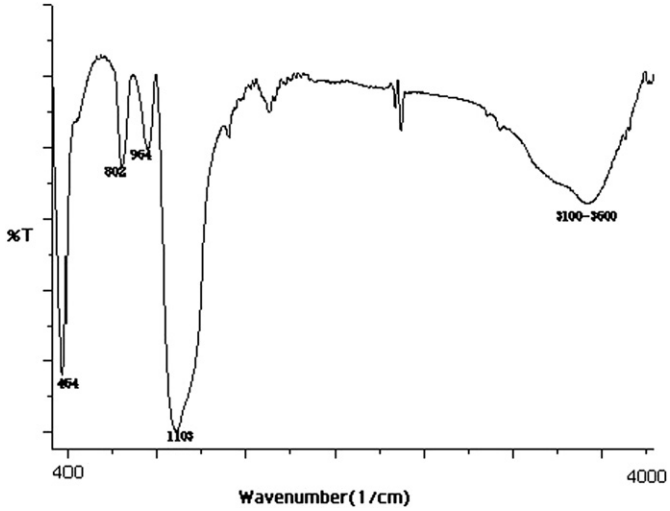

Fig. 2 FTIR spectrum of SNPs. The scanned wave number range is from 400–4000 cm^{-1}. The peaks are as follows: (1) 464 cm^{-1} (Si–O–Si bending), (2) 802 cm^{-1} (Si–O–Si symmetric stretching), (3) 964 cm^{-1} (Si–OH bending), (4) 1103 cm^{-1} (Si–O–Si asymmetric stretching), (5) 3100–600 cm^{-1} (Si–OH stretching).

achieved by changing only the concentration of NH_3 solution (6, 8, 12, 16, 20 and 24% v/v). It has been observed that a further increase in NH_3 solution concentration (from 24% v/v) could not produce remarkable change in particle size, showing a saturation effect.

Fig. 1a shows the electron diffraction pattern of SNPs. The ring structure obtained from the sample confirmed its amorphous nature. The chemical characterization for the nanoparticles was carried out by EDS analysis and EDS mapping as shown in Fig. 1b and c respectively. The results of chemical analysis revealed that four elements—C, O, Si and Cu, existed in SNPs (Fig. 1b). C and Cu peaks come from the carbon coated copper grid used for TEM and EDS analysis. In EDS mapping of Fig. 1c, red, blue and pink color indicated silica, oxygen and carbon (from the carbon supporting film on grid), respectively. EDS chemical analysis and mapping confirmed that the expected SNPs have successfully developed in this study.

The chemical structure of SNPs was studied using FT-IR spectroscopy as shown in Fig. 2. The peaks identified were: Si–O–Si bending at 464 cm^{-1}, Si–O–Si symmetric stretching vibration at 802 cm^{-1}, Si–OH bending vibration at 964 cm^{-1}, Si–O–Si asymmetric stretching vibration at 1103 cm^{-1} and a broad peak from 3100–3600 cm^{-1} due to Si–OH stretching vibration. The observed results agree with previously published results in the literatures [46–48] and this confirmed the similarity in structural characteristics of the developed SNPs by the present method.

SEM images showed small sized SNPs (about 5 nm) at low concentration of NH_3 solution (6% v/v) (Fig. 3A) and they appeared in agglomerated form. However a gradual increase

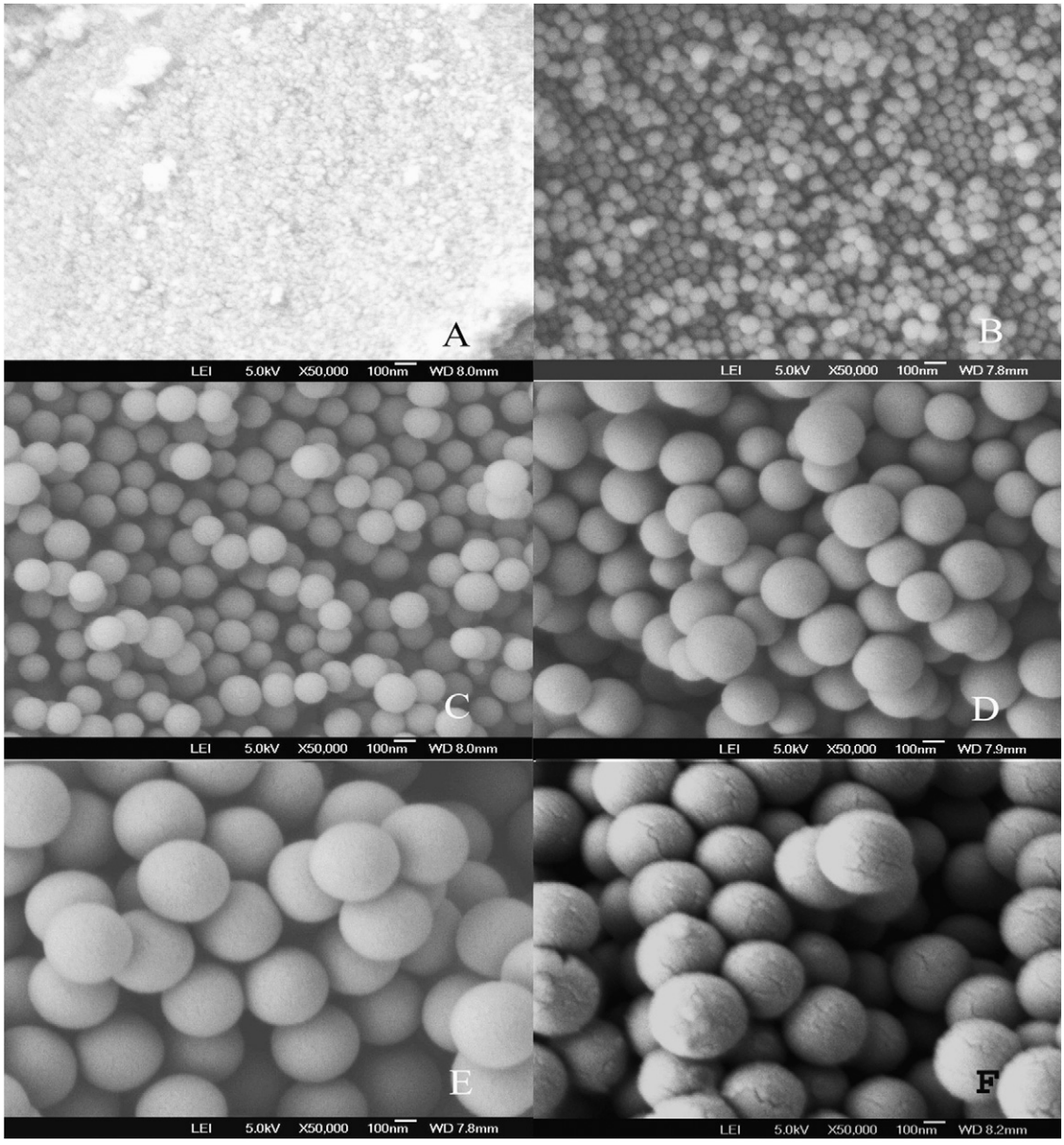

Fig. 3 SEM images of SNPs at different concentrations of NH_3 solution. (A) SNPs at 6% v/v NH_3 solution (Average diameter: 9.16 nm). (B) SNPs at 8% v/v NH_3 solution (Average diameter: 67.81 nm). (C) SNPs at 12% v/v NH_3 solution (Average diameter: 137.66 nm). (D) SNPs at 16% v/v NH_3 solution (Average diameter: 216.62 nm). (E) SNPs at 20% v/v NH_3 solution (Average diameter: 242.07 nm). (F) SNPs at 24% v/v NH_3 solution (Average diameter: 257.03 nm).

in the nanoparticle size was observed with a corresponding increase in the concentration of NH_3 solution (8, 12, 16, 20 and 24% v/v) and SNPs appeared as defined spherical shape and without obvious aggregation as shown in Fig. 3B–E. It was also noticed that the surface smoothness reduced with increased particle size (around 250 nm) as shown in Fig. 3F. The images obtained from TEM and SEM clearly showed that the synthesized SNPs were nearly monodisperse in nature and maintained their size in nanometer range. Fig. 4 shows a linear relationship between the size of nanoparticles and the concentration of NH_3 solution. It is clear that even after keeping all other parameters (concentration of TEOS, ethanol, water and reaction temperature) constant, the size of the nanoparticles increased with increase in the concentration of NH_3 solution alone. However, on reaching particle size about 250 nm (at 24% NH_3 solution), the particles size reached a saturation level no further increase in size has been found with corresponding increase in the concentration of NH_3 solution (28 and 32% v/v).

The synthesis process of SNPs involves hydrolysis and condensation reactions. Usually hydrolysis is a very slow process and the particle growth rate is limited by hydrolysis [18]. An acid or a base could act as a catalyst for hydrolysis reactions. In the base catalyzed synthesis of SNPs, ammonia catalyzes the hydrolysis step. Besides, ammonia promotes condensation reactions that result in a faster kinetics and thus increased particle size [49]. All these facts well explain the increase in nanoparticle size with corresponding increase in the concentration of NH_3 solution.

SNPs have to be made porous for the incorporation of suitable drugs to serve as an efficient drug delivery system [30–33]. To make SNPs suitable for drug delivery applications, the plasma treatment for generating pores on SNPs was conducted. Compared to the chemical etching and calcination processes, plasma etching is more acceptable due to the additional advantages like low processing temperature, non-wet method and very short treatment time is needed. Our aim was to generate pores on SNPs without using any structure directing

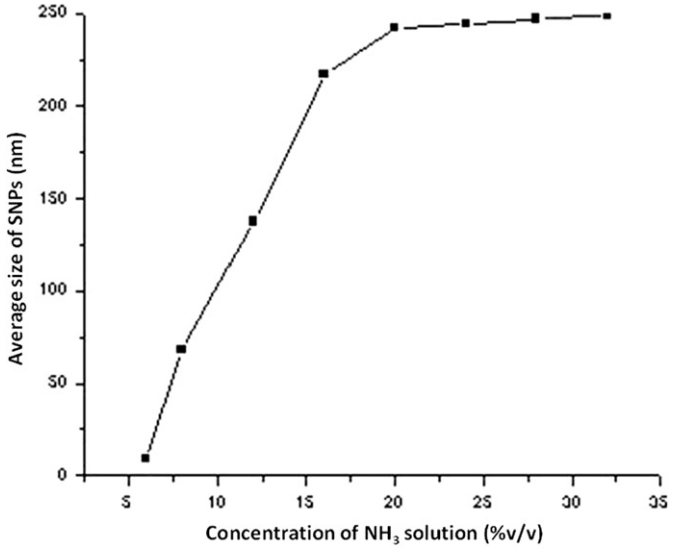

Fig. 4 Graph showing the relationship between the sizes of SNPs and the concentration of NH_3 solution. Keeping all other parameters constant, the size of the nanoparticles increased with corresponding increase in $NH_3 \cdot H_2O$ concentration. The size of the nanoparticles reached a saturation level at around 250 nm and further increase in ammonia concentration did not cause much increase in nanoparticle size.

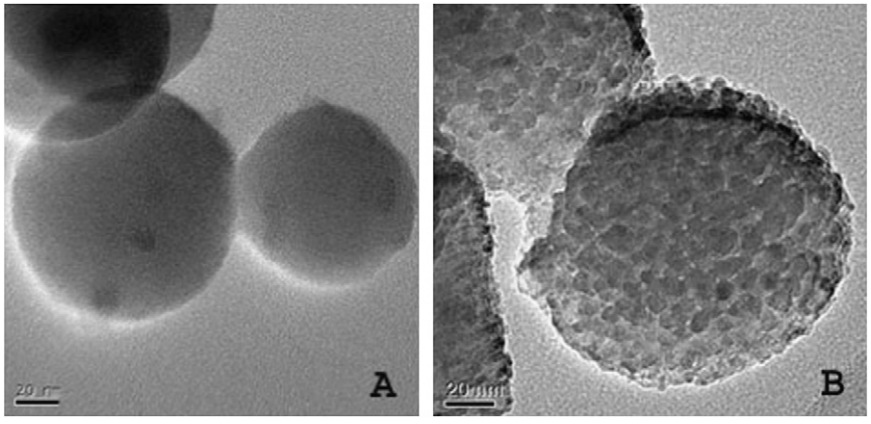

Fig. 5 TEM image of SNPs without (A) and with plasma treatment (B).

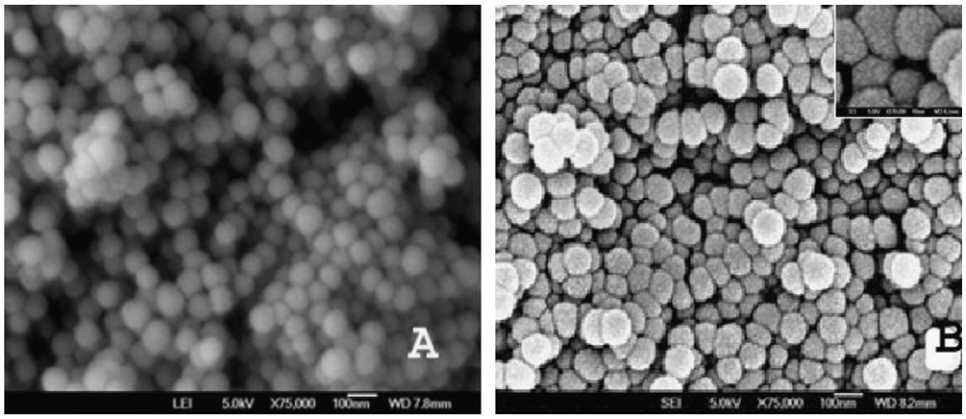

Fig. 6 SEM image of SNPs without (A) and with plasma treatment (B). (Inset shows higher magnification.) From the TEM and SEM images it was found that oxygen plasma etching was a successful tool for generating pores on SNPs.

agents or organic templates in the synthesis procedures because the free occurrence of such agents could break open the cell membranes [38,50] and hence their complete removal from SNPs should be assured to avoid any chance of cell toxicity during cellular delivery. Therefore the method developed in this study provides an easy and safe synthesis of porous SNPs. The characterization of argon plasma (at argon flow rate of 5 ml/min at 20 °C with 100–200 W processing power and varying processing time from 30 min to 1 h) treated samples failed to find any pores on the surface of SNPs in the cases of both without and with heating of 150 °C. Argon plasma treatment is a physical process in which the ionized gas dislodges the organic templates if any. Since no such organic templates had been used in the synthesis of SNPs, argon plasma was not successful enough to induce pores on SNPs. Our initial experiments with oxygen plasma (at a flow rate of 60 ml/min at 20 °C with same processing power and processing time as with argon plasma) without any sample heating were not successful in generating pores. However on heating the samples to 150 °C, we could successfully generate pores on the surface which is very clear from the TEM and SEM images. Figs. 5 and 6 show TEM and SEM images of SNPs without and with plasma etching. Formation of pores on the surface of SNPs was very clear from Figs. 5B and 6B. Hence, along with heating SNPs at 150 °C, oxygen plasma treatment (at 150 W for 30 min) was found to be a successful tool for generating pores on surface of nanoparticles. This might be due to the fact that oxygen plasma treatment is a chemical process and calcination in oxygen plasma could affect inorganic silica that might lead to pore generation on the surface of SNPs by surface etching [43,44]. The thus-synthesized porous silica nanoparticles can be loaded with suitable payloads by simple diffusive process and their controlled delivery in response to various stimuli can be achieved as similar to various reported literatures of MCM-41 mesoporous silica solid support [33,34,51].

4. Conclusions

The size of SNPs affects their physical, chemical, electrical and optical properties. Even though the preparation of different nanosized silica particles has been studied extensively, the development of a reliable, optimized and easy method for the synthesis of SNPs with size tunabilities is still needed.

Instead of varying different parameters (such as concentration of silica source, chain length and concentration of alcohol, concentration of morphological catalyst like ammonia, reaction temperature etc) for controlling nanoparticle synthesis and size, the authors have successfully prepared SNPs with a size range of 5–250 nm by controlling only one parameter i.e., the concentration of ammonia solution- in base-catalyzed synthesis method of SNPs. Such size tuned SNPs could be successfully used for drug delivery in animals and plant cells since most cellular uptake and translocation between cells occur successfully within this size range.

The pores on the surface of SNPs have successfully generated by oxygen plasma treatment, which can be used for the incorporation of suitable drugs. Oxygen plasma treatment along with sample heating (150 °C) was proved as a promising direct tool for pore creation thereby avoiding any additional organic templates or structure directing agents, which might be toxic to cells and living tissues and is currently in use for inducing pores on SNPs.

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References

[1] A. Corma, From microporous to mesoporous molecular sieve materials and their use in catalysis, Chemical Reviews 97 (1997) 2373–2419.
[2] C.-T. Wang, C.-L. Wi, I.C. Chen, Y.-H. Huang, Humidity sensors based on silica nanoparticle aerogel thin films, Sensors and Actuators B Chemical 107 (2005) 402–410.
[3] I.T. Kuo, Y.-F. Huang, H.T. Chang, Silica nanoparticles for separation of biologically active amines by capillary electrophoresis with laser-induced native fluorescence detection, Electrophoresis 26 (2005) 2643–2651.
[4] N.K. Mal, M. Fujiwara, Y. Tanaka, Photo controlled reversible release of guest molecules from coumarin-modified mesoporous silica, Nature 42 (2003) 350–353.
[5] T.K. Barik, B. Sahu, V. Swain, Nanosilica- from medicine to pest control, Parasitology Research 103 (2008) 253–258.
[6] I. Roy, T.Y. Ohulchansky, H.E. Pudavar, E.J. Bergey, A.R. Oseroff, J. Morgan, T.J. Dougherty, P.N. Prasad, Ceramic-based

nanoparticles entrapping water-insoluble photosensitizing anticancer drugs: a novel drug-carrier system for photodynamic therapy, Journal of the American Chemical Society 125 (2003) 7860–7865.
[7] Z.P. Xu, Q.H. Zeng, G.Q. Lu, A.B. Yu, Inorganic nanoparticles as carriers for effecient cellular delivery, Chemical Engineering Science 61 (2006) 1027–1040.
[8] C. Yague, M. Moros, V. Grazu, M. Arruebo, J. Santamaria, Synthesis and stealthing study of bare and PEGylated silica micro- and nanoparticles as potential drug-delivery vectors, Chemical Engineering Journal 137 (2008) 45–53.
[9] D. Luo, W.M. Saltzman, Thinking of silica, Gene Therapy 13 (2006) 585–586.
[10] T.K. Jain, I. Roy, T.K. De, A. Maitra, Nanometer silica particles encapsulating active compounds: a novel ceramic drug carrier, Journal of the American Chemical Society 120 (1998) 11092–11095.
[11] F. Torney, B.G. Trewyn, V.S.-Y. Lin, K. Wang, Mesoporous silica nanoparticles deliver DNA and chemicals into plants, Nature Nanotechnology 2 (2007) 295–300.
[12] D.J. Bharali, I. Klejbor, E.K. Stachowiak, P. Dutta, I. Roy, N. Kaur, E.J. Bergey, P.N. Prasad, M.K. Stachowiak, Organically modified silica nanoparticles: a non viral vector for in vivo gene delivery and expression in brain, Proceedings of the National Academy of Sciences of the USA 102 (2005) 11539–11544.
[13] C. Kneuer, M. Sameti, U. Bakowsky, T. Schiestel, H. Schirra, H. Schmidt, C.-M. Lehr, A non viral DNA delivery system based on surface modified silica nanoparticles can efficiently transfect cells in vitro, Bioconjugate Chemistry 11 (2000) 926–932.
[14] D.R. Radu, C.-Y. Lai, K. Jeftinija, E-W. Rowe, S. Jeftinija, V.S.-Y. Lin, A polyamidoaminedendrimer-capped mesoporous silica nanospheres- based gene transfection agent, Journal of the American Chemical Society 126 (2004) 13216–13217.
[15] C.-Y. Lai, B.G. Trewyn, D.M. Jeftinija, K. Jeftinija, X. Shu, S. Jeftinija, V.S.-Y. Lin, A mesoporous silica nanosphere-based carrier system with chemically removable CdS nanoparticle caps for stimuli–responsive controlled release of neurotransmitters and drug molecules, Journal of the American Chemical Society 125 (2003) 4451–4459.
[16] I.I. Slowing, J.L. Cvivero-Escoto, C.-W. Wu, V.S.-Y. Lin, Mesoporous silica nanoparticles as controlled drug delivery and gene transfection carriers, Advanced Drug Delivery Reviews 60 (2008) 1278–1288.
[17] E. Navarro, A. Baun, R. Behra, N.B. Hartmann, J. Filser, A-J. Miao, A. Quigg, P.H. Santschi, L. Sigg, Environmental behaviour and ecotoxicity of engineered nanoparticles to algae, plants and fungi, Ecotoxicology 17 (2008) 372–386.
[18] S.-L. Chen, P. Dong, G.-H. Yang, J-J. Yang, Kinetics of formation of monodisperse colloidal silica particles through the hydrolysis and condensation of tetraethylorthosilicate, Industrial and Engineering Chemistry Research 35 (1996) 4487–4493.
[19] H.-P. Lin, C.-P. Tsai, Synthesis of mesoporous silica nanoparticles from a low concentration CnTMAX-sodium silicate component, Chemistry Letters 32 (2003) 1092.
[20] X.-G. Lee, C. Oh, S.-K. Yoo, S-M. Koo, S.-G. Oh, New approach for the control of size and surface characteristics of mesoporous silica particles by using mixed surfactants in w/o emulsion, Microporous and Mesoporous Materials 86 (2005) 134–144.
[21] A.B.D. Nandiyanto, S-G. Kim, F. Iskandar, K. Okuyama, Synthesis of spherical mesoporous silica nanoparticles with nanometer-size controllable pores and outer diameters, Microporous and Mesoporous Materials 120 (2009) 447–453.
[22] A. Stober, A. Fink, E. Bohn, Controlled growth of monodisperse silica spheres in micron size range, Journal of Ccolloid and Interface Science 26 (1968) 62–69.
[23] G.H. Bogush, M.A. Tracy, C.F. Zukoski IV, Preparation of monodisperse silica particles: control of size and mass fraction, Journal of Non-Crystalline Solids 104 (1988) 95–106.
[24] T. Yokoi, Y. Sakomoto, O. Terasaki, Y. Kubota, T. Okubo, T. Tatsumi, Periodic arrangements of silica nanospheres assisted by aminoacids, Journal of the American Chemical Society 128 (2006) 13664–13665.
[25] K.D. Hartlen, A.P.T. Athanasopoulos, V. Kitaev, Facile preparation of highly monodisperse small silica spheres (15 to >200 nm) suitable for colloidal templating and formation of ordered arrays, Langmuir 24 (2008) 1714–1720.
[26] J. Guo, X. Liu, Y. Cheng, Y. Li, G. Xu, P. Cui, Size-controllable synthesis of monodispersed colloidal silica nanoparticles via hydrolysis of elemental silicon, Journal of Colloid and Interface Science 326 (2008) 138–142.
[27] A. Sousa, E.M.B. Sousa, Influence of synthesis temperature on the structural characteristics of mesoporous silica, Journal of Non-Crystalline Solids 352 (2006) 3451–3456.
[28] S.K. Park, K.D. Kim, H.T. Kim, Preparation of silica nanoparticles: determination of the optimal synthesis conditions for small and uniform particles, Colloids and Surfaces A 197 (2002) 7–17.
[29] G.-L. Davies, A. Barry, Y.K. Gun'ko, Preparation and size optimization of silica nanoparticles using statistical analyses, Chemical Physics Letters 468 (2009) 239–244.
[30] I.I. Slowing, B.G. Trewyn, S. Giri, S.-Y.V. Lin, Mesoporous silica nanoparticles for drug delivery and biosensing applications, Advanced Functional Materials 17 (2007) 1225–1236.
[31] J. Lu, M. Liong, J.I. Zink, F. Tamanoi, Mesoporous silica nanoparticles as a delivery system for hydrophobic anticancer drugs, Small 3 (2007) 1341–1346.
[32] J-F. Chen, H.-M. Ding, J.-X. Wang, L. Shao, Preparation and characterization of porous hollow silica nanoparticles for drug delivery application, Biomaterials 25 (2004) 723–727.
[33] E. Anzar, M.D. Marcos, M.-M. Ramon, F. Sancenon, J. Soto, P. Amoros, C. Guillem, pH and photo-switched release of guest molecules from mesoporous silica supports, Journal of the American Chemical Society 131 (2009) 6833–6843.
[34] N.M. Khashab, A. Trabolsi, Y.A. Lau, M.W. Ambrogio, D.C. Friedman, H.A. Khatib, J.I. Zink, J.F. Stoddart, Redox- and pH-controlled mechanized nanoparticles, European Journal of Organic Chemistry (2009) 1669–1673.
[35] D.P. Ferris, Y.-L. Zhao, N.M. Khashab, H.A. Khatib, J.F. Stoddart, J.I. Zink, Light-operated mechanized nanoparticles, Journal of the American Chemical Society 131 (2009) 1686–1688.
[36] B.G. Trewyn, I.I. Slowing, S. Giri, H.-T. Chen, S.-Y.V. Lin, Synthesis and functionalization of a mesoporous silica nanoparticle based on the sol–gel process and application in controlled release, Accounts of Chemical Rresearch 40 (2007) 846–853.
[37] D.-W. Lee, S.-K. Ihm, K.H. Lee, Mesoporous silica framed by sphere-shaped silica nanoparticles, Microporous and Mesoporous Materials 83 (2005) 262–268.
[38] C.J. Murphy, A.M. Gole, J.W. Stone, P.N. Sisco, A.M. Alkilany, E.C. Goldsmith, S.C. Baxter, Gold nanoparticles in biology: beyond toxicity to cellular imaging, Accounts of Chemical Research 41 (2008) 1721–1730.
[39] S. Wang, W. Lu, O. Tovmachenko, U.S. Rai, H. Yu, P.C. Ray, Challenge in understanding size and shape dependent toxicity of gold nanomaterials in human skin keratinocytes, Chemical Physics Letters 463 (2008) 145–149.
[40] T. Niidome, M. Yamagata, Y. Okamoto, Y. Akiyama, H. Takahashi, T. Kawano, Y. Katayama, Y. Niidome, PEG-modified gold nanorods with a stealth character for in vivo applications, Journal of Controlled Release 114 (2006) 343–347.
[41] J. Zhang, A. Palaniappan, X. Su, F.E.H. Tay, Mesoporous silica thin films prepared by argon plasma treatment of sol–gel derived precursor, Applied Surface Science 245 (2005) 304–309.
[42] A. Palaniappan, J. Zhang, X. Su, F.E.H. Tay, Preparation of mesoporous silica films using sol–gel process and argon plasma treatment, Chemical Physics Letters 395 (2004) 70–74.
[43] J.M. Gomez-Vega, K. Teshima, A. Hozumi, H. Sugimura, O. Takai, Mesoporous silica thin films produced by calcination in

oxygen plasma, Surface and Coatings Technology 169–170 (2003) 504–507.
[44] H. Li, T. Kunitake, Efficient proton conduction of nanometer-thick film of porous silica as prepared by oxygen plasma treatment, Microporous and Mesoporous Materials 97 (2006) 42–48.
[45] D. SakthiKumar, K. Nakamura, A. Shoji, Y. Yoshida, Cobalt tetraphenylporphine (CoTPP) film as glucose and hydrogen peroxide sensors after immobilizing glucose oxidase (GOx), Sensors and Materials 18 (2006) 339–352.
[46] J.M. Kim, S.M. Chang, S.M. Kong, K-S. Kim, J. Kim, W.-S. Kim, Control of hydroxyl group content in silica particle synthesized by the sol–gel precipitation process, Ceramics International 35 (2009) 1015–1019.
[47] I.A. Rahman, P. Vejayakumaran, C.S. Sipaut, J. Ismail, C.K. Chee, Size-dependent physiochemical and optical properties of silica nanoparticles, Materials Chemistry and Physics 114 (2009) 328–332.
[48] T.-S. Deng, Q.-F. Zhang, J.-Y. Zhang, X. Shen, K-T. Zhu, J-L. Wu, One-step synthesis of highly monodisperse hybrid silica spheres in aqueous solution, Journal of Colloid and Interface Science 329 (2009) 292–299.
[49] K.-S. Kim, J.-K. Kim, W.-S. Kim, Influence of reaction conditions on sol-precipitation process producing silicon oxide particles, Ceramics International 28 (2002) 187–194.
[50] E.E. Connor, J. Mwamuka, A. Gole, C.J. Murphy, M.D. Wyatt, Gold nanoparticles are taken up by human cells but do not cause acute toxicity, Small 1 (2005) 325–327.
[51] S. Angelos, N.M. Khashab, Y.-W. Yang, A. Trabolsi, H.A. Khatib, J.F. Stoddart, J.I. Zink, pH clock-operated mechanized nanoparticles, Journal of the American Chemical Society 131 (2009) 12912–12914.